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MUSTARD, LEWISITE, AND PHOSGENE OXIME BURNS ON THE DEPILATED SKIN OF A HEIFER TO DETERMINE THE ANIMAL'S VESICATING POTENTIAL

by

J. M. Maas, Captain, M.C.
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ARMY CHEMICAL CENTER, MARYLAND

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CHEMICAL CORPS
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Mustard, Lewisite, and Phosgene Oxime Burns on the Depilated Skin of a Heifer to Determine the Animal's Vesicating Potential

ABSTRACT

Predictable vesication does not occur in the bovine species following exposure to mustard, lewisite, and phosgene oxime.

Lesions resulting from lewisite are more severe and heal more slowly than mustard lesions in the bovine species.

Medical Laboratories Research Report No. 350

Mustard, Lewisite, and Phosgene Oxime Burns on the Depilated Skin of a Heifer to Determine the Animal's Vesicating Potential

I. INTRODUCTION.

A. Object.

To determine the vesicating potential of the depilated skin of the heifer.

B. Authority.

Authorized by the Chief Chemical Officer under Cml C Project No. 4-59-12-007, Clinical Investigation and Treatment of CW Casualties in Man, Cml C Research and Development Program for fiscal year 1954.

II. HISTORICAL.

Extensive investigations (1-14) to determine the vesicating producing potential of vesicants on various species of animals indicate the condition cannot be precisely duplicated in the manner observed in human subjects. Pseudo-vesication manifesting itself as a somewhat greater accumulation of fluid in the corium has been observed in the skin of the bird and frog following exposure to a vesicant. Lactating bitches exposed to vesicants developed blisters on and in the area immediately adjacent to the teats. Very young (suckling) pigs demonstrate lesions superficially resembling vesication in man when mustard or lewisite is applied percutaneously. The inferences are clear, however, that in many of the experiments reported in the literature, predictable responses proved to be the rare exception. Furthermore, the pseudo-vesication observed in frogs and birds differs sufficently from true vesication noted in human subjects, so that such animals cannot be utilized for certain definitive test projects where precisely comparable pathological conditions should exist.

III. EXPERIMENTAL.

A. Methods and Materials.

To the best of our knowledge, the bovine species has heretofore not been investigated for vesicant-producing potentiality following exposure to mustard or lewisite. As a prelude to a project to select the most desirable test animal for use in screening certain new decontaminants and protective agents against established preparations, it was speculated that a young calf might be ideal for the purpose. This consideration was based on the premise that heifers and all cloven-footed animals exhibit typical vesication in the development of cowpox lesions.

A study was therefore proposed to apply mustard, lewisite, and phosgene oxime in liquid and vapor states to the depilated skin of a heifer to determine whether vesication would occur.

Two test sites were decided upon to permit application of the vesicants in vapor and liquid form. The Edgewood Vapor Cup developed at these laboratories was selected for application of the three agents in gaseous states. Simple cotton-tipped orange-stick swabs were decided upon to apply each agent in its liquid form.

A Holstein heifer approximately six months old was used for the experiment. Three days before the test application, the ventral surface of the abdomen just anterior to the udder was bilaterally depilated with strontium sulfate. This procedure provoked cutaneous irritation characterized by erythema, and, subsequently, pin-point areas of bleeding. Photographs 1 and 2 depict the test sites 72 hours post depilation. It is possible that the irritated areas may have been increasingly susceptible to the subsequent action of the vesicants.

Laboratory "pure" sulfur mustard, lewisite, and phosgene oxime were procured from Cml C Chemical & Radiological Laboratories. Orange sticks tipped with a minute amount of cotton were dipped in the individual solutions, and excesses carefully removed by gentle pressure. Vapor cups were prepared by applying one drop of solution to blotter paper affixed in the base of the cup.

B. Results.

The test was instituted at 1000 hours, 24 August 1953. Atmospheric conditions prevailing were: Temperature, 74°F.; relative humidity, 65%. The animal was roped, thrown, and then constrained. The right abdomen was tested initially. Lewisite (98.3%) was applied to the skin by swab and permitted to remain in place one minute. Phosgene oxime (70%) was then similarly applied to a site approximately 5 inches caudad and laterally. Finally, a swab containing mustard (95%) was placed in contact with the denuded skin, approximately 6 inches caudad and laterally to the phosgene oxime site.

A vapor cup containing lewisite was placed on a pre-selected point of the denuded test area on the left abdominal wall. Air currents within the cup were induced by means of rotating a paper "fan" attached to an orange stick protruding from the hollow stem of the cup. Phosgene oxime and mustard applications were carried out in a similar manner with each test site located approximately 5 inches caudad and lateral to the previously tested area. In each instance the vapor cup was kept in place for a five minute period. The application of phosgene oxime apparently was accompanied by extreme discomfort inasmuch as the animal bellowed lustily when this agent was applied.

Photographs 3 (right) and 4 (left) taken one hour after completion of the applications are not revealing. The cup margins of the

lewisite exposure (photograph 4) are demarcated by a pale halo. Other exposed areas are not readily discernible. Six hours after exposure, the lewisite lesion on the right revealed a pustular area 3 cm. in diameter. An area of edema 10 by 30 cm. radiated outward from the core of the lesion. The phosgene oxime wound was circumscribed, white, 3 cm. in diameter, with slight erythema extending beyond. The mustard lesion was characterized by a slightly erythematous area 4 to 5 cm. in diameter. The lesions on the left side were essentially similar to those on the right with the exception that the cup edges on the lewisite lesion were demarcated by a pale ring (photograph 4) and the edematous area was somewhat smaller (8 by 25 cm.). Daily observations were made and recorded. To avoid needless repetition, only those pertinent changes appearing chronologically will be described. Dates of individual observations will show number of days elapsed since exposure.

25 August 1953 - 24 hours post exposure

1. Right Side.

a. Lewisite: The general area of the test has an appearance of marked subcutaneous edema. In an area which corresponds to the limits of the swab used to apply the agent, the skin has a yellowish-gray appearance representing coagulation necrosis. The area just described is surrounded to a distance of 2 cm. by a reddish-purple discoloration believed to be hemorrhagic congestion. It seems at this point that the agent has spread to and involves the erythematous area of depilation where there is evidence of irregular, dark brownish-purple discoloration.

b. Phosgene oxime: The involved area corresponds in size to the original test site. There is a dark yellowish-brown discoloration probably representing necrosis. No other obvious reaction apparent.

c. Mustard: The lesion is grey in color and corresponds in size to the initial test area of the swab site. Extending slightly beyond the wound is an irregular, marginal erythema, purple in color.

2. Left Side.

a. Lewisite: The cup margin is clearly demarcated by a pale rim of necrotic tissue. The inner area of the cup site further shows hemorrhagic discoloration without slough. A similar area of discoloration surrounds the primary lesion for a distance of 6 cm. The extensive subcutaneous edema present 6 hours after the exposure, persists and involves the phosgene oxime lesion as well.

b. Phosgene oxime: The lesion is purplish-black and corresponds to the size of the cup used to produce it. Obvious breakdown of tissue is not apparent.

c. Mustard: The lesion is represented only as an erythematous area corresponding to the size of the vapor cup. There is no evidence of subcutaneous edema.

3. Photographs.

a. Right Side, no. 5, 24 hours post exposure.

b. Left Side, no. 6, 24 hours post exposure.

4. Thirty hours post exposure. A large, pendulous sac, 8 by 10 cm. in diameter, and 8 cm. deep, is present in the midline of the abdomen. It is speculated that this sac represents edematous fluid having drained from the lesion sites, particularly from the lewisite areas.

26 August 1953 - 48 hours post exposure

1. Right Side.

a. Lewisite: The original area of necrosis is essentially as seen at 24 hours. At this point there are now irregular extensions of greyish discoloration which are believed to represent necrotic changes. The hemorrhagic erythema areas are darker and browner in color; and more firm in consistency. There appears to be somewhat less edema.

b. Phosgene oxime: The lesion is unchanged in size but darker in color. It is firm in consistency.

c. Mustard: The mustard area is unchanged in size, but definitely browner in color, and with an increase in consistency. Localized edema, not previously present, is now evident.

2. Left Side.

a. Lewisite: The area maintains the same dimensions as previously described. The rim area of necrosis is somewhat more sharply demarcated. The hemorrhagic, necrotic area has taken on a deep brown color, but with some evidence of redness still remaining. Edema has subsided considerably and is less pronounced than on the right side.

b. Phosgene oxime: The area is the same in size as previously noted. The site has acquired a deep brown color.

c. Mustard: The area is unchanged in size. It is only barely distinguishable by a faint erythema.

3. Photographs.

a. Right Side, no. 7, 48 hours post exposure.

b. Left Side, no. 8, 46 hours post exposure.

4. Edema. The bulk of the edema of both areas has shifted to a midline position. Inherent weight and gravity predisposes to a midline sacculation.

27 August 1953 - 72 hours post exposure

1. Right Side.

a. Lewisite: The swab area shows in addition to the greyish-yellow coagulation site, certain areas of blotchy, brown discoloration. The margins of the central swab area are no longer as distinct as previously. The peripheral zone of the previous hemorrhagic erythema has become very dark reddish-brown in color. There is suggestive evidence of newly forming subcutaneous edema.

b. Phosgene oxime: This area has acquired a deep brown color. Its contour is slightly depressed and somewhat concave.

c. Mustard: The swab area is dark brown in color. Definite evidence of subcutaneous edema exists.

2. Left Side.

a. Lewisite: The rim area of coagulation necrosis shows slight brownish discoloration. The cuff area and border of the rim are almost black. There is no change in extent of edema.

b. Phosgene oxime: The area is somewhat darker in color but otherwise unchanged.

c. Mustard: The area can no longer be discerned.

3. Photographs.

a. Right Side, no. 9, 72 hours post exposure.

b. Left Side, no. 10, 72 hours post exposure.

4. Edema. Midline edema has abated to approximately 50% of that previously described.

28 August 1953 - 96 hours

1. Right Side.

a. Lewisite: The swab site is barely distinguishable. The entire area, including the marginal spread, has assumed a relatively uniform, very dark, reddish-brown color. Along the periphery there is evidence of separation which suggests a superficial slough. Edema in the immediate area is unchanged.

b. Phosgene oxime: The entire area is dark brown in color. The upper margin shows signs of separation indicating a superficial slough.

c. Mustard: The area is somewhat more brown in color than previously described. There is evidence of very early separation at the margins. The edema described earlier has abated somewhat.

2. Left Side.

a. Lewisite: The color previously discussed persists in an unchanged condition. Only a small portion of the lesion from the cup rim is discernible. The entire lesion has acquired a definite depressed character. There is evidence of superficial separation at the margin. Edema is more pronounced.

b. Phosgene oxime: The area shows no change from the preceding day.

3. Photographs.

a. Right Side, no. 11, 96 hours post exposure.

b. Left Side, no. 12, 96 hours post exposure.

4. Edema. The edematous sacculation in the midline persists.

5. General Appearance. A slight but definite weight loss is visually perceptible. The discomfort the animal experiences probably precludes appetite, and/or feeding.

1 September 1953 - 8 days

1. Right Side.

a. Lewisite: The lesion is covered by a dirty gray eschar. Edema is subsiding.

b. Phosgene oxime: As for Lewisite.

c. Mustard: As for Lewisite.

2. Left Side.

a. Lewisite: As for lewisite on right side.

b. Phosgene oxime: As for lewisite.

3. Edema. No change in degree or character of midline edema.

3 September 1953 - 10 days

1. Right Side.

a. All lesions similar in appearance to previous description.

2. Left Side.

a. Lewisite: The surface appearance is unchanged. There is definite evidence of resuming edema represented by an area 8 cm. in diameter and 3 cm. thick.

b. Phosgene oxime: The area shows no change from that previously described.

8 September 1953 - 15 days

1. Right Side.

a. Lewisite: No change.

b. Phosgene oxime: The eschar became detached while palpating the wound. The underlying surface is clean, pink, and shows no points of bleeding.

c. Mustard: No change.

2. Left Side.

a. Lewisite: The edema persists.

b. Phosgene oxime: No change in the lesion.

11 September 1953 - 18 days

1. Right Side.

a. All lesions essentially static in character.

2. Left Side.

a. Lewisite: The edema appears to be subsiding. The eschar remains intact.

b. Phosgene oxime: The eschar previously present apparently became detached spontaneously. The base of the wound is clean, pink in color, not tender, and shows no points of bleeding.

21 September 1953 - 28 days

1. Right Side.

a. Lewisite: The eschar is firm, hard, dirty-gray in color. There is no further progression of the detaching process described earlier.

b. Mustard: The eschar remains intact.

2. Left Side.

a. Lewisite: As for right side.

7 October 1953 - 44 days

1. Right Side.

a. Lewisite: The eschar shows evidence of detaching spontaneously. Dark yellow-red purulent exudate exudes from the exposed wound edges.

b. Mustard: The eschar shows early signs of spontaneous detachment.

2. Left Side.

a. Lewisite: The eschar remains intact.

12 October 1953 - 49 days

1. Right Side.

a. Lewisite: The eschar has become detached spontaneously. The surface of the wound shows presence of deep brown, thick, purulent material. The ulcer wall is clearly demarcated. There is evidence of recent bleeding. The crater is estimated to be 3/8 inch deep.

b. Mustard: The eschar has become detached. The base of the underlying wound is pink, clean, not tender, and shows no recent points of bleeding.

2. Left Side.

a. Lewisite: The eschar remains intact.

13 October 1953 - 50 days

1. Right Side.

a. Lewisite: The purulent discharge is still present, but reduced in quantity.

15 October 1953 - 52 days

1. Right Side.

a. Lewisite: The purulent discharge is no longer present. The base of the wound is deep red in color.

2. Left Side.

a. Lewisite: No change from earlier description.

19 October 1953 - 56 days

1. Right Side.

a. Lewisite: The wound is approximately 1 1/8 inches in diameter and about 3/8 inch deep. The edges are well demarcated. The base is clean, and pink in color.

22 October 1953 - 59 days

1. Right Side.

a. Lewisite: A new eschar has formed. The new eschar is thin, about 1¼ inches in diameter and is dirty grey in color.

2. Left Side.

a. Lewisite: No change from previous description.

3 November 1953 - 71 days

1. Right Side.

a. Lewisite: The eschar has again spontaneously detached. The base of the wound is clean, pink in color, dry, and shows no points of bleeding.

2. Left Side.

a. Lewisite: The eschar shows early signs of detachment.

5 November 1953 - 73 days

1. Left Side.

a. Lewisite: The eschar remains attached at one corner only. The crater of the wound is approximately 2 inches in diameter, and 3/8 inch deep. The walls are clearly demarcated. Extensive, deep yellow-brown, thick purulent exudate is present together with a small quantity of almost black, residual blood. The area is not tender to palpation.

9 November 1953 - 77 days

1. Right Side.

a. Lewisite: The wound shows evidence of slow progressive healing. There is no indication of new eschar formation.

2. Left Side.

a. Lewisite: The eschar is completely detached. The area of the ulcer is somewhat smaller and shallower. Exudation is minimal. There is no evidence of new eschar formation.

12 November 1953 - 80 days

1. Right Side.

a. Lewisite: The lesion is completely healed.

2. Left Side.

a. Lewisite: The crater is replaced by granulation tissue. The area is slightly tender and bleeds readily. There is no evidence of exudate or new eschar formation.

16 November 1953 - 84 days

1. Left Side.

a. Lewisite: A thin eschar has again formed on the lesion. The lesion is approximately 1½ inches long, ¼ inch wide. The color is dirty gray.

23 November 1953 - 91 days

1. Left Side.

a. Lewisite: The eschar has become detached. The wound surface is pink, clean, and shows no points of bleeding.

27 November 1953 - 95 days

1. Right Side.

a. All test areas have acquired an appearance comparable to surrounding tissue.

2. Left Side.

a. As above.

IV. CONCLUSIONS.

1. Heifers do not predictably develop blisters following application of vesicants.

2. Lewisite was found to produce lesions of far greater severity and which healed far more slowly than mustard or phosgene oxime in at least this single test animal of the bovine species.

3. Application of phosgene oxime to the depilated skin of the test animal was accompanied by immediate intense pain.

4. Because of difficulty in handling, the bovine species is not an ideal animal to employ for test purposes such as this experiment consisted of.

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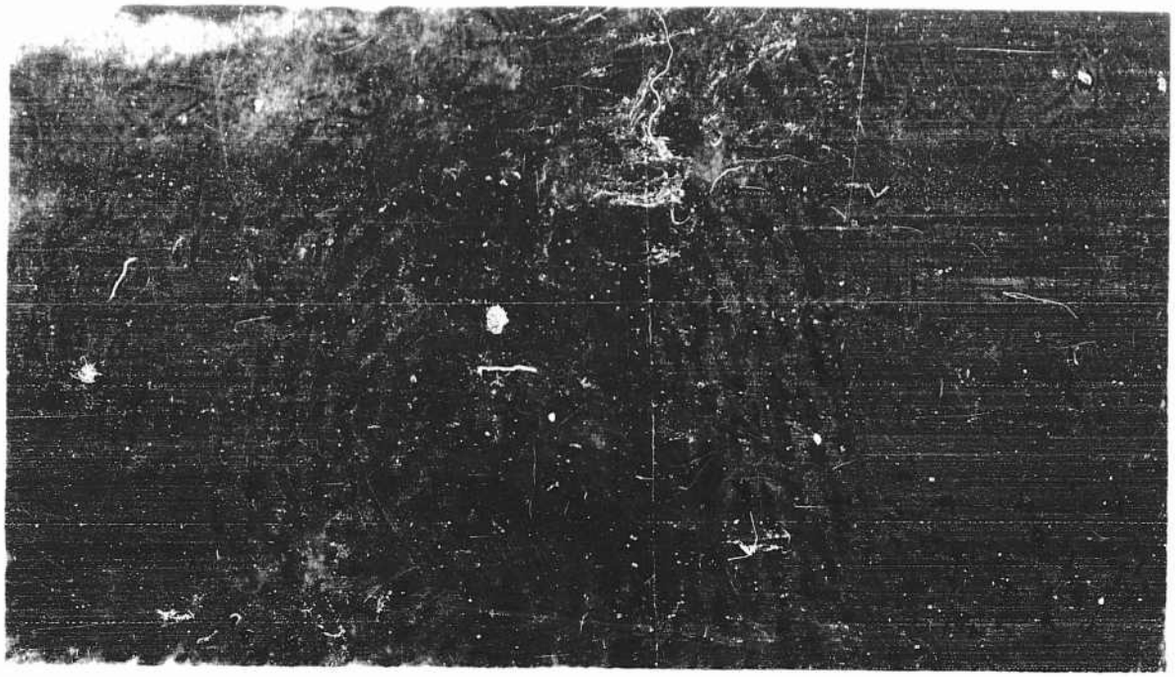
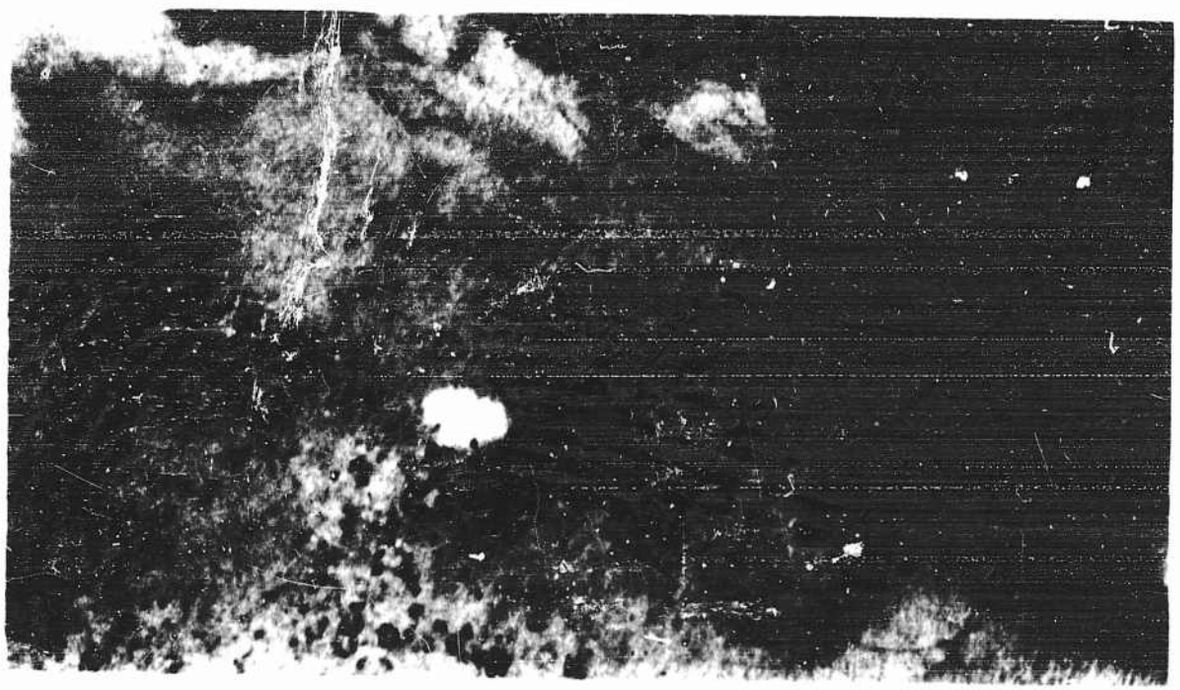


Photograph 1

Test site 72 hours post depilation.



Photograph 2

Test site 72 hours post depilation.

Photograph 3

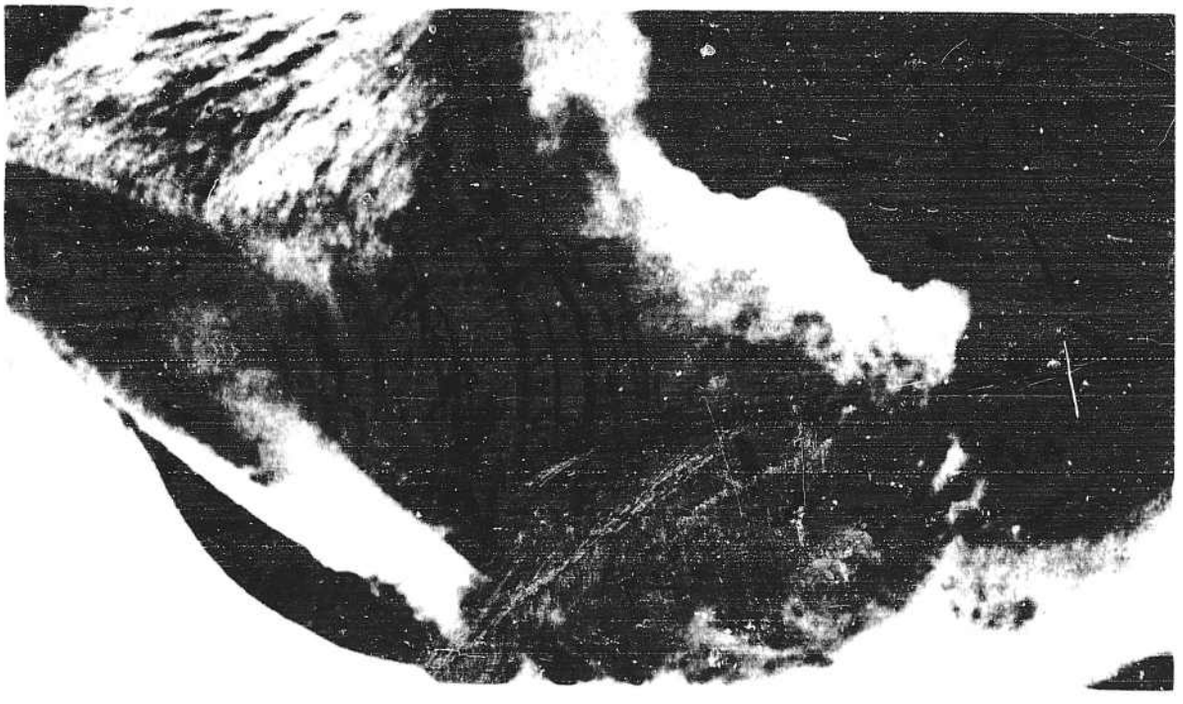
Right side, one hour post application of vesicant, not revealing.

Photograph 4

Left side, one hour post application of vesicant. Cup margins of lewisite exposure are demarcated by a pale halo.

Photograph 5

Right side, 24 hours post exposure.

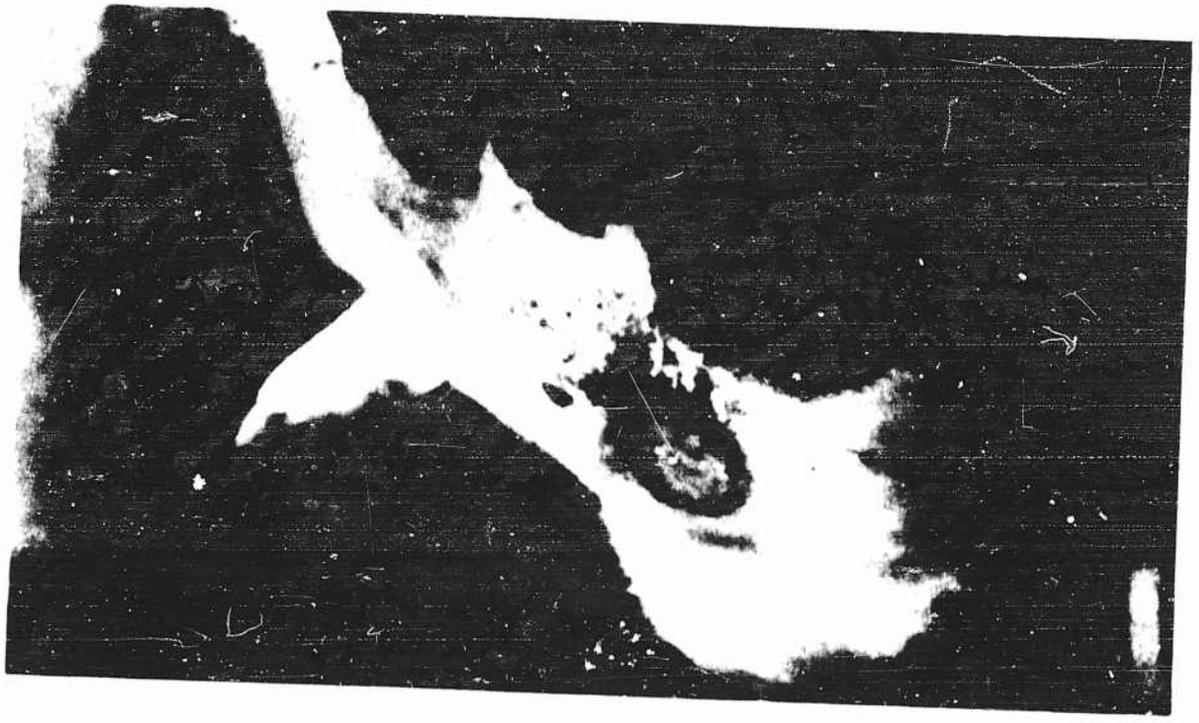


Photograph 6

Left side, 24 hours post exposure.

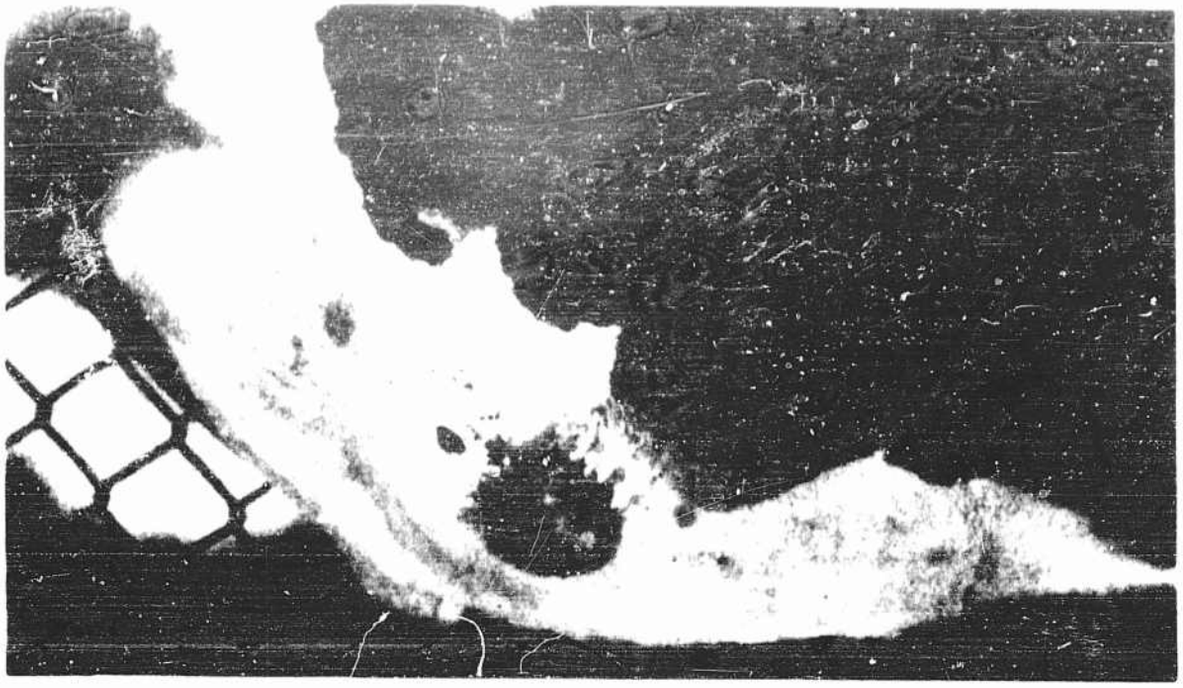
Photograph 7

Right side, 48 hours post exposure.



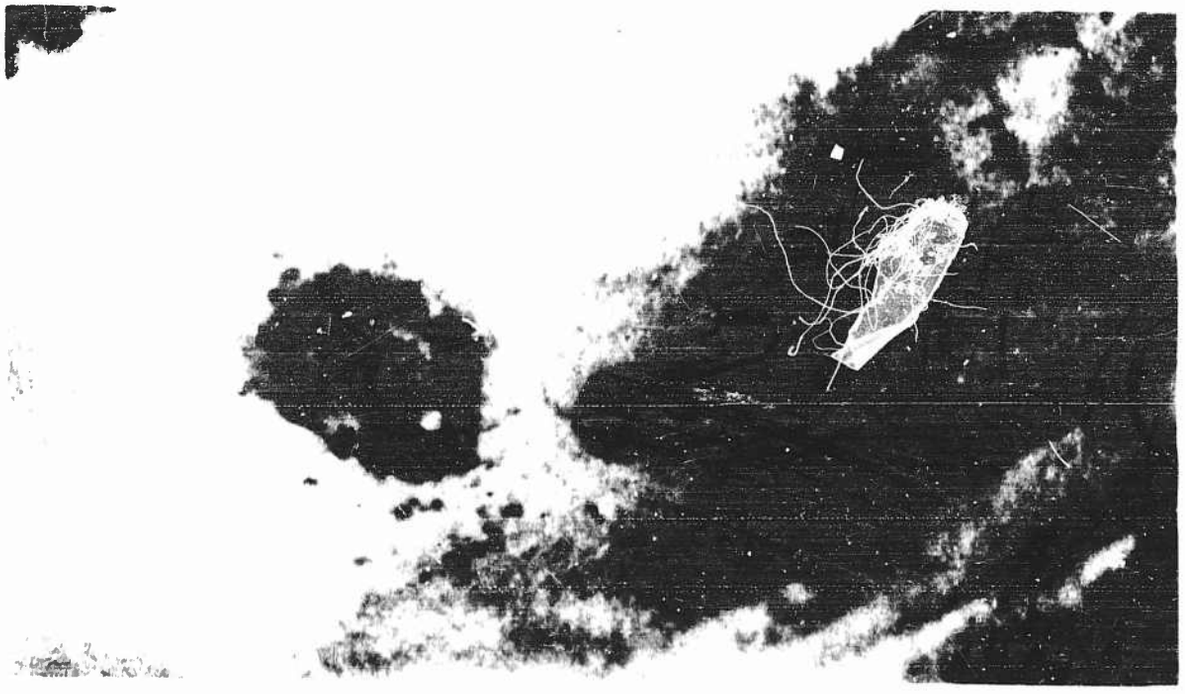
Photograph 8

Left side, 48 hours post exposure.



Photograph 9

Right side, 72 hours post exposure.

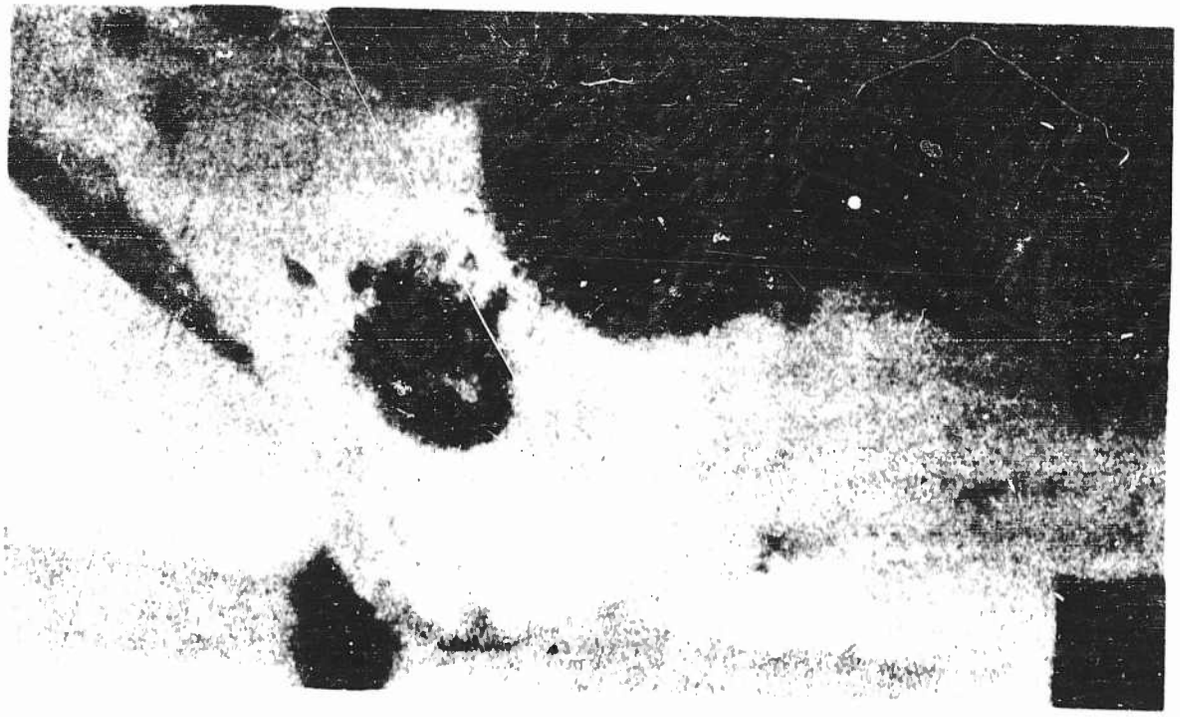


Photograph 10

Left side, 72 hours post exposure.

Photograph 11

Right side, 96 hours post exposure.



Photograph 12

Left side, 96 hours post exposure.

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SUBMITTED:

J. M. MAAS, Captain, M.C.*
Clinical Investigation Branch

A. J. McADAMS, Captain, M.C.*
Pathology Branch

WILLIAM P. McSHANE*
Clinical Investigation Branch

* Authors

Authority:

Project No. 4-59-12-007

APPROVAL RECOMMENDED:

GUSTAVE FREEMAN, M. D.
Chief, Clinical Investigation Branch

J. M. M. INNES
Chief, Pathology Branch

AMEDEO S. MARRAZZI, M.D.
Chief, Clinical Research Division

Typed: 17 March 1955
jch

APPROVED:

for DAVID B. DILL
Scientific Director
Chairman, Publications Committee

NORMAN W. ELTON
Colonel, Medical Corps
Commanding

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SUGGESTED TOPICS FOR INDEXING MEDICAL LABORATORIES RESEARCH REPORT NO. 350

1. Lewisite, physiol. effects, depilated skin
2. Mustard, physiol. effects, depilated skin
3. Phosgene oxime, physiol. effects, depilated skin